

## WEST Search History

DATE: Tuesday, September 30, 2003

### Set Name Query

side by side

### Hit Count Set Name

result set

*DB=USPT; PLUR=YES; OP=ADJ*

L9	L8 and insulin	10	L9
L8	L4 and arachidonic acid	25	L8
L7	L4 and imidazolacetic acid	1	L7
L6	L4 and iarachidonic acid	0	L6
L5	L4 and imidazolacetic acid	1	L5
L4	L3 and cell	832	L4
L3	L2 and receptor	856	L3
L2	L1 and imidazol\$	1423	L2
L1	((530/388.22  530/388.21 )!.CCLS.  (514/43 )!.CCLS.  (435/6  435/7.2  435/7.9 )!.CCLS.  (536/26.9 )!.CCLS. )	14043	L1

END OF SEARCH HISTORY

(FILE 'HOME' ENTERED AT 13:24:36 ON 30 SEP 2003)

FILE 'REGISTRY' ENTERED AT 13:24:41 ON 30 SEP 2003

L1           STRUCTURE UPLOADED  
L2           0 S L1 SSS SAM  
L3           5 S L1 SSS FULL

FILE 'CAPLUS, MEDLINE, USPATFULL' ENTERED AT 13:25:33 ON 30 SEP 2003

L4           28 S L3  
L5           0 S L3 AND IMIDAZOLINE  
L6           26 S L3 AND IMIDAZOL?

L6 ANSWER 1 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:715348 CAPLUS

DOCUMENT NUMBER: 123:103310

TITLE: **Imidazoleacetic** acid, a .gamma.-aminobutyric acid receptor agonist, can be formed in rat brain by oxidation of histamine

AUTHOR(S): Thomas, Boban; Prell, George D.

CORPORATE SOURCE: Dep. Pharmacol., Mt. Sinai Sch. Med. City Univ. New York, New York, NY, USA

SOURCE: Journal of Neurochemistry (1995), 65(2), 818-26

CODEN: JONRA9; ISSN: 0022-3042

PUBLISHER: Lippincott-Raven

DOCUMENT TYPE: Journal

LANGUAGE: English

AB It is generally accepted that in mammalian brain histamine is metabolized solely by histamine methyltransferase (HMT), to form tele-methylhistamine, then oxidized to tele-methylimidazoleacetic acid. However, histamine's oxidative metabolite in the periphery, **imidazoleacetic** acid (IAA), is also present in brain and CSF, and its levels in brain increase after inhibition of HMT. To reinvestigate if brain has the capacity to oxidize histamine and form IAA, conscious rats were injected with [3H]histamine (10 ng), either into the lateral ventricles or cisterna magna, and decapitated 30 min later. In brains of saline-treated rats, most radioactivity recovered was due to tele-methylhistamine and tele-methylimidazoleacetic acid. However, significant amts. of tritiated IAA and its metabolites, IAA-ribotide and IAA-riboside, were consistently recovered. In rats pretreated with metoprine, an inhibitor of HMT, labeled IAA and its metabolites usually comprised the majority of histamine's tritiated metabolites. [3H]Histamine given intracisternally produced only trace amts. of oxidative metabolites. Formation of IAA, a potent GABA-A agonist with numerous neurochem. and behavioral effects, from minute quantities of histamine in brain indicates a need for reevaluation of histamine's metabolic pathway or pathways in brain and suggests a novel mechanism for interactions between histamine and the GABAergic system.

L6 ANSWER 2 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1992:470204 CAPLUS

DOCUMENT NUMBER: 117:70204

TITLE: Nucleosides. 163. Synthesis of ribosides and ribotides of **imidazole-4(5)-acetic** acid and 1-methylimidazole-4(5)-acetic acid

AUTHOR(S): Matulic-Adamic, Jasenka; Watanabe, Kyoichi A.

CORPORATE SOURCE: Lab. Org. Chem., Sloan-Kettering Inst. Cancer Res., New York, NY, 10021, USA

SOURCE: Korean Journal of Medicinal Chemistry (1991), 1(1), 54-64

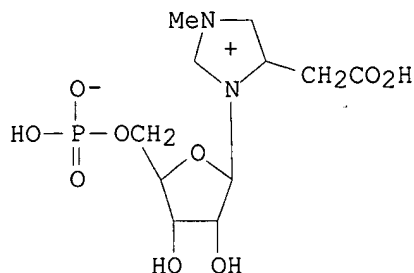
CODEN: KJMCE7; ISSN: 1225-0058

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 117:70204

GI



AB Nucleotide **imidazoleacetic** acid, e.g. I, were prepd. from **imidazole-4(5)-acetonitrile** (II). Regioselective tritylation of II followed by N-methylation with Me<sub>2</sub>S and hydrolysis gave 1-methylimidazole-5-acetic acid.

L6 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1984:18260 CAPLUS

DOCUMENT NUMBER: 100:18260

TITLE: Catabolism of histamine in the isolated glomeruli and tubules of the rat kidney

AUTHOR(S): Abboud, Hanna E.

CORPORATE SOURCE: Dep. Med., Case West. Res. Univ., Cleveland, OH, USA

SOURCE: Kidney International (1983), 24(4), 534-41

CODEN: KDYIA5; ISSN: 0085-2538

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Rat kidney glomeruli and cortical tubules were incubated with radiolabeled histamine [51-45-6], and the products were sepd. by TLC. Glomeruli predominantly catabolized histamine to acid metabolites of the diamine oxidase (histaminase) pathway, **imidazole** acetic acid [645-65-8] and ribosylimidazole acetic acid [29605-99-0], and to a lesser extent to the inactive methylation product, N.tau.-methylhistamine [501-75-7]. Tubules, on the other hand, catabolized histamine to N.tau.-methylhistamine and to a lesser degree to acid metabolites. The Me donor S-adenosyl-methionine (SAM) (10-4M) markedly enhanced the prodn. of N.tau.-methylhistamine in both glomeruli and tubules but had no effect on the prodn. of acid metabolites. In the presence of equimolar concns. of SAM, tubules continued to methylate histamine to a greater extent than glomeruli. In both glomeruli and tubules, the diamine oxidase inhibitor, amino-guanidine, abolished the prodn. of acid metabolites whereas amodiaquine and pyrilamine, inhibitors of the methylation pathway, markedly reduced the prodn. of N.tau.-methylhistamine. In the presence of SAM, tubules catabolized nonlabeled histamine to a greater extent than glomeruli. Thus, tubules have a greater capacity than glomeruli to degrade histamine and histamine is differentially catabolized in these segments. A major pathway of histamine catabolism in glomeruli results in the formation of biol. active products.

L6 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1983:138012 CAPLUS

DOCUMENT NUMBER: 98:138012

TITLE: Biliar elimination of histamine and its metabolites in guinea pigs

AUTHOR(S): Puerta, M. L.; Ballester, M. E. M.

CORPORATE SOURCE: Fac. Cienc. Biol., Univ. Complutense Madrid, Madrid, Spain

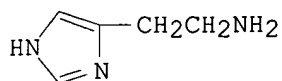
SOURCE: Comparative Biochemistry and Physiology, C: Comparative Pharmacology (1983), 74C(1), 111-13

CODEN: CBPCBB; ISSN: 0306-4492

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB Administration of <sup>14</sup>C-labeled histamine (I) [51-45-6] i.v. to guinea pigs resulted in 3.5% of the radioactivity being eliminated in the bile of both males and females. Free I, methylhistamine [501-75-7], methimidazoleacetic acid [2625-49-2], **imidazoleacetic** acid [645-65-8] and its riboside [29605-99-0], and acetylhistamine [673-49-4] were identified in the bile. Male bile contained more free I and methylhistamine than did female bile. Evidently, biliary elimination of I and metabolites is similar to that of urine but quant. less important.

L6 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1978:48665 CAPLUS

DOCUMENT NUMBER: 88:48665

TITLE: Histamine metabolism in cluster headache and migraine.  
Catabolism of <sup>14</sup>C-histamine

AUTHOR(S): Sjaastad, Ottar; Sjaastad, O. V.

CORPORATE SOURCE: Dep. Neurol., Rikshosp., Oslo, Norway

SOURCE: Journal of Neurology (1977), 216(2), 105-17

CODEN: JNRYA9; ISSN: 0340-5354

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Various parameters of histamine metab. were studied in patients with migraine, cluster headache, and chronic paroxysmal hemicrania. These included urinary excretion of radioactivity and of histamine-<sup>14</sup>C and its metabolites, exhaled <sup>14</sup>CO<sub>2</sub> and fecal radioactivity after oral as well as s.c. administration of histamine-<sup>14</sup>C. No marked deviation from the normal was found except in 1 patient with the cluster headache variant, chronic paroxysmal hemicrania, in whom an aberration in histamine degrading seemed to be present. Only min. quantities of the histamine-<sup>14</sup>C metabolite **imidazoleacetic**-<sup>14</sup>C acid riboside seemed to be formed during severe paroxysms. During a symptom-free period no deviation from normal was obsd. The most likely explanation for this finding seems to be a defect in the conversion of **imidazoleacetic** acid to its riboside. This defect may possibly explain the increased urinary excretion of histamine in this particular patient. The relation of this metabolic aberration to the prodn. of headache still remains dubious for various reasons.

L6 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1977:101217 CAPLUS

DOCUMENT NUMBER: 86:101217

TITLE: Histamine and its metabolites in cat portal venous blood and intestine after duodenal instillation of histamine

AUTHOR(S): Marley, E.; Thomas, D. V.

CORPORATE SOURCE: Dep. Pharmacol., Inst. Psychiatry, London, UK

SOURCE: Journal of Physiology (Cambridge, United Kingdom)

(1976), 263(2), 273P-274P

CODEN: JPHYA7; ISSN: 0022-3751

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Histamine [51-45-6] (0.175-0.220 mg/kg) instilled into the intestine of cats was metabolized mainly in the intestinal wall by either diamine oxidase [9001-53-0]-deamination or by **imidazole** N-methylation followed by monoamine oxidase [9001-66-5]-deamination. I.v. infused

histamine (0.15 .mu.g/kg/min) was metabolized mainly by methylation at sites other than the intestine. Deamination by diamine oxidase was delayed in the absence of the gut and liver.

L6 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1976:553943 CAPLUS  
DOCUMENT NUMBER: 85:153943  
TITLE: Interference with histamine and **imidazole**  
acetic acid metabolism by salicylates: a possible  
contribution to salicylate analgesic activity?  
AUTHOR(S): Beaven, M. A.; Horakova, Zdenka; Keiser, H. R.  
CORPORATE SOURCE: Natl. Heart Lung Inst., NIH, Bethesda, MD, USA  
SOURCE: Experientia (1976), 32(9), 1180-2  
CODEN: EXPEAM; ISSN: 0014-4754  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB In man, rats and mice, the urinary excretion of the histamine [51-45-6] and the L-histidine [71-00-1] metabolite, **imidazole** acetic acid [645-65-8], was increased and that of the conjugated metabolite, ribosylimidazole acetic acid [29605-99-0], decreased by small doses of salicylates. In contrast to salicylates, other non-salicylate anti-inflammatory drugs, indomethacin [53-86-1], phenylbutazone [50-33-9], phenacetin [62-44-2] and acetaminophen [103-90-2] did not influence the excretion of the urinary metabolites of histamine and L-histidine. Since **imidazole** acetic acid is reported to have analgesic and narcotic activity, there is the inference that the analgesic properties of salicylate might be due in part to interference in **imidazole** acetic acid metab.

L6 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1975:166843 CAPLUS  
DOCUMENT NUMBER: 82:166843  
TITLE: Ion exchange chromatography for quantitative analysis  
of radioactive histamine metabolites in human urine  
AUTHOR(S): Bergmark, J.; Granerus, G.  
CORPORATE SOURCE: Dep. Clin. Chem., Univ. Goteborg, Goteborg, Swed.  
SOURCE: Scandinavian Journal of Clinical and Laboratory  
Investigation (1974), 34(4), 365-73  
CODEN: SJCLAY; ISSN: 0036-5513  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The method was compared with the isotope diln. method developed by R. W. Schayer (1959). The advantages of the new method are rapidity and a greater possibility to account for all the radioactive histamine metabolites excreted in the urine. Data also suggested that the histamine metabolite, **imidazoleacetic** acid riboside, is partly lost in the isotope diln. method because of adsorption to urinary constituents during hydrolysis. The catabolism of i.v. and orally given histamine-14C was studied in one healthy subject. The general metabolic pattern of histamine was confirmed. In addn., it was found that histaminol might be a minor metabolite of injected histamine.

L6 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1974:115938 CAPLUS  
DOCUMENT NUMBER: 80:115938  
TITLE: Catabolism of orally administered carbon-14-labeled  
histamine in man  
AUTHOR(S): Sjaastad, Ottar; Sjaastad, O. V.  
CORPORATE SOURCE: Inst. Surg. Res., Univ. Hosp., Oslo, Norway  
SOURCE: Acta Pharmacologica et Toxicologica (1974), 34(1),  
33-45  
CODEN: APTOA6; ISSN: 0001-6683  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Within 48 hr following oral administration of 14C-labeled histamine-2HCl (I-2HCl) [56-92-8] (.sim.200 mg) to humans, 68-80% of the radioactivity was recovered in the urine, 1.8-18% was exhaled as 14CO2, and 13-19% was excreted in the feces. The main urinary I metabolites were **imidazoleacetic** acid [645-65-8] and methylimidazoleacetic acid [2625-49-2].

L6 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1973:146963 CAPLUS

DOCUMENT NUMBER: 78:146963

TITLE: Differentiation of 1,4- and 1,5-disubstituted **imidazoles**

AUTHOR(S): Matthews, H. Randall; Rapoport, Henry

CORPORATE SOURCE: Lawrence Berkeley Lab., Univ. California, Berkeley, CA, USA

SOURCE: Journal of the American Chemical Society (1973), 95(7), 2297-303

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A method is presented for distinguishing 1,4- and 1,5-disubstituted **imidazoles** by their proton cross-ring coupling consts. Other spectral methods also have been evaluated, as well as several methods which have been reported for differentiating such isomers. Comparison of these methods leads to the conclusion that the measurement of cross-ring coupling consts. is the most generally satisfactory and reliable procedure. On this basis, structures are assigned to the carboxymethylhistidines, and the histamine metabolite is established as 1-.beta.-d-ribofuranosyl-4- **imidazoleacetic** acid.

L6 ANSWER 11 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1971:137653 CAPLUS

DOCUMENT NUMBER: 74:137653

TITLE: Metabolism of [14C]-histamine in domestic animals. II. Cow and sheep

AUTHOR(S): Eliassen, K. A.

CORPORATE SOURCE: Dep. Physiol., Vet. Coll. Norway, Oslo, Norway

SOURCE: Acta Physiologica Scandinavica (1971), 81(3), 289-99

CODEN: APSCAX; ISSN: 0001-6772

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB In cow and sheep the oxidative deamination of histamine (I) into **imidazoleacetic** acid and its riboside was the major metabolic pathway. About 2% of the urinary radioactivity following 14C-labeled I injection was due to histaminol.

L6 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1971:74587 CAPLUS

DOCUMENT NUMBER: 74:74587

TITLE: Uptake of [14C]-histamine by tissues of the guinea pig

AUTHOR(S): Lewis, A. J.; Nicholls, Paul J.

CORPORATE SOURCE: Welsh Sch. Pharm., UWIST, Cardiff, UK

SOURCE: Journal of Pharmacy and Pharmacology (1971), 23(1), 66

CODEN: JPPMAB; ISSN: 0022-3573

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB The low uptake of ring-2-14C-labeled histamine (I) (80 mg/kg, i.v.) by various tissues of guinea pigs showed that the animal, unlike cats and rabbits, does not possess an effective uptake system. The acidic metabolites of I, when detd. 8 hr after the administration, were identified as **imidazole**-4-acetic acid, 1-ribosylimidazole-4-acetic acid, and 1-methylimidazole-4-acetic acid.

L6 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1965:441136 CAPLUS  
DOCUMENT NUMBER: 63:41136  
ORIGINAL REFERENCE NO.: 63:7422g-h  
TITLE: Evidence for the presence of **imidazoleacetic** acid riboside and ribotide in rat tissues  
AUTHOR(S): Robinson, Joseph D.; Green, Jack P.  
CORPORATE SOURCE: School of Med., Yale Univ.  
SOURCE: Federation Proceedings (1965), 24(3;1), 777  
CODEN: FEPR7; ISSN: 0014-9446  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A combination of ion-exchange and paper chromatography of the acid-sol. radioactive material from kidneys of rats given histamine-14 C showed the presence of **imidazoleacetic** acid riboside (I) and ribotide (II) and a third unidentified substance whose Rf value differed from all known metabolites of histamine. The most likely route for the synthesis of I and II would be oxidn. of histamine to **imidazoleacetic** acid followed by condensation of the acid with phosphoribosyl pyrophosphate, a reaction demonstrated in vitro; the I would then arise by dephosphorylation. Labeled histamine adenine dinucleotide and histamine adenine dinucleotide phosphate could not be detected in kidney, liver, or brain.

L6 ANSWER 14 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1965:441135 CAPLUS  
DOCUMENT NUMBER: 63:41135  
ORIGINAL REFERENCE NO.: 63:7422e-g  
TITLE: Methylhistamine in urine and brain  
AUTHOR(S): Fram, D. H.; Green, J. P.  
CORPORATE SOURCE: School of Medicine, Yale Univ.  
SOURCE: Federation Proceedings (1965), 24(3;1), 778  
CODEN: FEPR7; ISSN: 0014-9446  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Methylhistamine (1-methyl-4-( $\beta$ -amino-ethyl)-**imidazole**) (I), found as a normal const. of urine and brain, was measured by prep. its deriv. with 1-fluoro-2,4-dinitro-benzene (II) from acid exts. of urine or brain. The method was validated qual. by submitting the acid ext. to paper, thin-layer, ion-exchange, or gas chromatography and by submitting derivs. prep. from the exts. with II, 2-fluoro-3-bromo-4,6-dinitro-benzene, 1-chloro-2,4,6-trinitrobenzene, or 2,4-dichloro-5-nitro-pyrimidine to paper or thin-layer chromatography. The 24-hr. urinary excretion of I in normal humans was 137-480  $\mu$ g.; histamine excretion was 16-53  $\mu$ g. The ratio of I to histamine excreted ranged from 6 to 15. There was no sex difference in the excretion of either amine or in the ratios. The concn. of I in the brain of guinea pig was 45-75  $\mu$ g./g.

L6 ANSWER 15 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1964:486555 CAPLUS  
DOCUMENT NUMBER: 61:86555  
ORIGINAL REFERENCE NO.: 61:15113g-h  
TITLE: Presence of **imidazoleacetic** acid riboside and ribotide in rat tissues  
AUTHOR(S): Robinson, J. D.; Green, J. P.  
CORPORATE SOURCE: Yale Univ., School of Med., New Haven, CT  
SOURCE: Nature (London, United Kingdom) (1964), 203(4950), 1178-9  
CODEN: NATUAS; ISSN: 0028-0836  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable

AB In rats given multiple injections of labeled histamine (I), chromatography



of trichloroacetic acid (TCA) exts. of kidney revealed 3 major radioactive fractions. These were **imidazoleacetic** acid riboside (II), **imidazoleacetic** acid ribotide (III) and an unidentified fraction not coinciding with any of the urinary I metabolites. In brain, after injection of labeled histidine (IV), chromatography of TCA exts. revealed small fractions of total tissue radioactivity in II, III, I and **imidazoleacetic** acid, higher levels in unidentified metabolites, and at least 80% as IV. Radioactivity from injected I or IV was not incorporated into histamine adenine dinucleotide (HAD) or HAD phosphate in rat or guinea pig organs.

L6 ANSWER 16 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1964:471247 CAPLUS  
DOCUMENT NUMBER: 61:71247  
ORIGINAL REFERENCE NO.: 61:12423e-h  
TITLE: The fate of histamine-14C in animal tissues  
AUTHOR(S): Snyder, Solomon H.; Axelrod, Julius; Bauer, Hugo  
CORPORATE SOURCE: Natl. Insts. of Health, Bethesda, MD  
SOURCE: Journal of Pharmacology and Experimental Therapeutics  
(1964), 144(3), 373-9  
CODEN: JPETAB; ISSN: 0022-3565  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable

AB Adult mice were administered histamine-2-14C (I) intravenously. There was a rapid initial disappearance of I. Methylhistamine-14C (II) concn. was max. at 30 min. After 90 min. I and II disappeared at a slower rate but could be detected in the whole animal at 48 hrs. After 48 hrs. the total radioactivity was twice the sum of I and II. After 30 min. the concn. of II was the same or higher than that of I in most tissues. The ratio of II to I was greatest in the spleen. I was not found in the brain. In all tissues total radioactivity exceeded the sum of I and II. The ratio of total radioactivity to the sum of I and II was greatest in the liver and kidney, and least in the spleen, blood, skeletal muscle, and stomach. Liver and kidney had the greatest concn. of total activity. Adult rats of both sexes received I subcutaneously and were killed 1 or 24 hrs. later. Negligible amts. of II were found. In all tissues total activity exceeded the concn. of I at 1 and 24 hrs. At both times total activity was greatest in the kidney and the ratio to I was larger than in other tissues. After 1 hr. kidney and heart had the greatest concn. of I while brain, serum, and testes had the least. After 24 hrs. the spleen had the largest amt. of I and its ratio of total activity to I was lowest. There were detectable levels of I and total activity in serum after 24 hrs. **Imidazoleacetic** acid (III) and **imidazoleacetic** acid riboside (IV) were found in equal concns. At 90 min. and at 4 hrs. their concns. exceeded those of I and II. After 48 hrs. the sum of I and II equaled the sum of III and IV. After 1 hr. there was a larger amt. of III in heart, lung, intestine, and spleen; the kidney and liver had a greater concn. of IV. After 24 hrs. the above tissues contained 10 times as much IV as III. Methylimidazoleacetic acid-14 C was not found. The amts. of I found in the brain of the rat indicated that I would cross the blood-brain barrier.

L6 ANSWER 17 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1964:456802 CAPLUS  
DOCUMENT NUMBER: 61:56802  
ORIGINAL REFERENCE NO.: 61:9880f-h, 9881a  
TITLE: Increased turnover of phosphoribosylpyrophosphate, a purine nucleotide precursor, in certain gouty subjects  
AUTHOR(S): Wyngaarden, J. B.; Jones, O. W.; Ashton, D. M.  
SOURCE: Atti Congr. Lega Intern. Reumatismo, 10.degree., Rome (1961), 1, 249-53  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Since phosphoribosylpyrophosphate (I) is an obligatory precursor of purine

nucleotides, its turnover has been investigated in gouty subjects. The hyperuricemia of gout may be due to overproduction or underexcretion of uric acid, or both. Orally administered **imidazoleacetic acid** (II) is partially excreted in urine as the **imidazoleacetic acid** ribonucleotide (III), and if glucose-14C is given simultaneously the ribose moiety is labeled. It is assumed that the same "pool" of I is involved both in the production of III and of phosphoribosylamine (the 1st specific precursor of purine nucleotides). Subjects were all males. Five controls had no gout or renal disease personally, or in the family history. Five gouty patients varied from asymptomatic hyperuricemia to advanced chronic tophaceous gout. All were given 25 .mu.c. glucose-U-14C and 20 micromoles/kg. II. Urine was collected in 5 ml. of concd. HCl, either in 2-hr. aliquots, or in a single 10-hr. sample, and stored at 4.degree.. CO2 was then removed by aeration, the pH adjusted to 8, the III collected on a Dowex-1 (acetate) column, and purified on a Dowex-50 (H+) column. The product in M citrate, pH 6.0, was hydrolyzed with a bacterial riboside hydrolase, and the protein-free filtrate passed through a mixed-bed resin (MB-3, Fisher), and the eluate analyzed for 14C and ribose (orcinol). Uric acid was detd. by differential spectrophotometry using uricase. In the controls, 0.010-0.047% 14C was incorporated into urinary III in 10 hours. For 2 gouty subjects with low and normal uric acid excretions, the corresponding figures were 0.009 and 0.058%, and for 3 gouty hyperuricemic subjects the range was 0.1640.309%. In these latter 3 subjects, the sp. activity (counts/ min./mg.) of the ribose moiety of III was approx. 8 times that of the controls. If urine were collected in 2-hr. aliquots, the max. sp. activity occurred about 2 hrs. earlier in all gouty subjects than in controls, and the peak values for the 3 hyperexcretors were 2-4-fold greater than controls. There was an increased I turnover in the 3 hyperexcretor gouty subjects, but there may be a continuous gradation in the magnitude of purine synthesis in man.

L6 ANSWER 18 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1962:465523 CAPLUS  
 DOCUMENT NUMBER: 57:65523  
 ORIGINAL REFERENCE NO.: 57:13071h-i  
 TITLE: Enzymic synthesis of a riboside involved in histamine metabolism  
 AUTHOR(S): Fernandes, J. F.; Castellani, Olga; Plese, Mitzi  
 CORPORATE SOURCE: Univ. Sao Paulo Med. School, Brazil  
 SOURCE: Ciencia Cult. (Sao Paulo) (1961), 13(No. 2), 87-92  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Unavailable

AB Exts. from the small intestine mucosa of the dog catalyzed reactions between histamine and **imidazole** acetate with 5-phosphoribosyl pyrophosphate. Exts. from the ileum and from the lung of the guinea pig also catalyzed these reactions, which required the presence of adenosine phosphate and of phosphate ions. A method for the purification and characterization of the products is presented.

L6 ANSWER 19 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1962:79591 CAPLUS  
 DOCUMENT NUMBER: 56:79591  
 ORIGINAL REFERENCE NO.: 56:15596b-h  
 TITLE: Synthesis of 1-(.beta.-D-ribofuranosyl)  
**imidazole**-4(or 5)-acetonitrile,  
 1-(.beta.-D-ribofuranosyl)**imidazole**-4(or  
 5)-acetic acid, and 4(or 5)-(2-aminoethyl)-1-(.beta.-D-  
 ribofuranosyl)**imidazole**  
 AUTHOR(S): Bauer, Hugo  
 CORPORATE SOURCE: Natl. Insts. of Health, Bethesda, MD  
 SOURCE: Journal of Organic Chemistry (1962), 27, 167-70  
 CODEN: JOCEAH; ISSN: 0022-3263  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Unavailable

AB cf. CA 53, 6214a. Condensation of the HgCl<sub>2</sub> complex (I) of **imidazoleacetonitrile** (II) with 2,3,5-tri-O-benzoyl-D-ribose bromide (III) and subsequent debenzoylation gave 1-(.beta.-D-ribofuranosyl)**imidazole**-4(or 5)acetonitrile (IV), converted by hydrolysis or catalytic hydrogenation to the corresponding acid (V) and histamine ribose (VI). II (2.14 g.) and 2.12 g. Na<sub>2</sub>CO<sub>3</sub> in 150 ml. hot H<sub>2</sub>O contg. 3 g. Celite stirred with addn. of 5.43 g. HgCl<sub>2</sub> in 150 ml. hot H<sub>2</sub>O, the centrifuged ppt. washed twice with H<sub>2</sub>O, dried at 70.degree. in vacuo, freed from moisture by azeotropic distn. with xylene, suspended in 150 ml. xylene, the suspension gently refluxed 3 hrs. with stirring with III (prepd. from 9 g. 2,3,5-tri-O-benzoyl-.beta.-D-ribose) in 100 ml. xylene, the xylene evapd. from the filtered soln., the light brown oil (VII) washed with Et<sub>2</sub>O, the insol. residue (5 g.) taken up in hot alc., the cooled soln. decanted, and the chilled liquid dild. with petr. ether yielded 1.6 g. HgCl<sub>2</sub> complex, (C<sub>31</sub>H<sub>25</sub>N<sub>3</sub>O<sub>7</sub>)<sub>2</sub>.HgCl<sub>2</sub>, m. 95.degree.. VII in CH<sub>2</sub>Cl<sub>2</sub> shaken with 30% aq. KI, the CH<sub>2</sub>Cl<sub>2</sub> soln. evapd., the residual oil taken up in alc., pptd. by addn. of petr. ether, and the middle fraction dried in vacuo at 45.degree. yielded 1-(2,3,5-tri-O-benzoyl-.beta.-D-ribose)-**imidazole**-4(or 5)-acetonitrile HCl salt (VIII), softening at 90.degree.. VII (10 g.) shaken in CH<sub>2</sub>Cl<sub>2</sub> with 30% aq. KI, the dried CH<sub>2</sub>Cl<sub>2</sub> soln. evapd., the oil taken up in 25 ml. MeOH, kept 16 hrs. at 20.degree. with 10 ml. 2N (MeO)<sub>2</sub>BA, the soln. adjusted to Congo red with 2N H<sub>2</sub>SO<sub>4</sub>, centrifuged, the supernatant washed with Et<sub>2</sub>O, freed from volatile materials, the soln. (IX) adsorbed on Dowex 50, eluted with 1 l. 2N H<sub>2</sub>SO<sub>4</sub>, the eluate treated with Ba(OH)<sub>2</sub>, the neutral soln. made slightly alk. with 10% NH<sub>4</sub>OH, evapd. at 30.degree. in vacuo, the residue taken up in H<sub>2</sub>O, decolorized (Norit) at room temp., evapd., the colorless gum (1.7 g.) taken up in abs. alc., the filtered soln. evapd., the product purified by soln. in alc. and filtration of the cooled soln., the filtrate evapd. in vacuo, washed with Me<sub>2</sub>CO, and dried gave hydrated IV, C<sub>10</sub>H<sub>13</sub>N<sub>3</sub>O<sub>4</sub>.H<sub>2</sub>O, with slight hydrolysis of the CN group. IV reacted with 1 equiv. NaIO<sub>4</sub> on titration showing the presence of 1 mole ribose. IX boiled 2 hrs. with 15 g. Ba(OH)<sub>2</sub> in 150 ml. H<sub>2</sub>O with evolution of NH<sub>3</sub>, treated with 2N H<sub>2</sub>SO<sub>4</sub>, the decolorized filtrate chromatographed on Dowex 1 acetate, eluted gradually with 3N AcOH to give material contg. free **imidazoleacetic** acid, the following fractions acidified with 2N HCl, the soln. evapd., and the residue (1.5 g.) recrystd. from H<sub>2</sub>O-Me<sub>2</sub>CO yielded VI HCl salt, m. 135%, [.alpha.]<sub>D</sub><sup>20</sup> -37.degree. (c 1.0, H<sub>2</sub>O), -51.4.degree. (c 1.16, MeOH), infrared spectrum in Nujol identical with that of a compd. isolated from the urine of rats injected with histamine or **imidazoleacetic** acid (CA 49, 11135b). II (1.07 g.) in 20 ml. alc. and 2 ml. concd. H<sub>2</sub>SO<sub>4</sub> hydrogenated 30 hrs. with shaking with 0.1 g. prereduced PtO<sub>2</sub>, the mixt. adsorbed on Dowex 50, and eluted with 4N HCl gave 1.0 g. histamine di-HCl salt. VII (50 ml.) acidified with 0.5 ml. concd. H<sub>2</sub>SO<sub>4</sub>, hydrogenated with 0.3 g. prereduced PtO<sub>2</sub> added in 2 portions, the acid removed as BaSO<sub>4</sub>, the soln. percolated through Dowex 50 H<sup>+</sup>, the column eluted with 2N HCl, and the product crystd. from H<sub>2</sub>O-Et<sub>2</sub>O gave VI di-HCl salt, m. 174-5.degree..

L6 ANSWER 20 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1962:74743 CAPLUS

DOCUMENT NUMBER: 56:74743

ORIGINAL REFERENCE NO.: 56:14584b-d

TITLE: The catabolism of tissue nucleic acid. III. The catabolism of ribonucleic acid after total-body x-irradiation

AUTHOR(S): Gerber, Georg B.; Gerber, Gisela; Altman, Kurt I.

CORPORATE SOURCE: Univ. of Rochester, Rochester, NY

SOURCE: International Journal of Radiation Biology and Related Studies in Physics, Chemistry and Medicine (1961), 4, 67-73

CODEN: IJRBA3; ISSN: 0020-7616

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. CA 54, 25159h. The effect of total-body x-irradiation on ribonucleic acid (RNA) catabolism was studied in rats whose RNA had been labeled by injection of glucose-U-C14 three days previously. The sp. activity of urinary ribosyl **imidazole** acetate (I) as well as of RNA of liver, intestine, muscle, spleen and thymus was detd. after x- or sham-irradiation. Rats were either pair fed or starved after irradiation. After 1000 r. the sp. activity of I was increased whereas that of intestinal and muscle RNA was decreased with little change in liver RNA. In pair-fed animals, exposure to 756 r. decreased the sp. activity of spleen and thymus RNA, and gave a steady decrease in that of I over 5 days. Sp. activity of liver RNA was diminished in the sham-irradiated rats and was equiv. to that of I which was excreted on the first day after treatment. It was concluded that radiation-induced increase in RNA catabolism is present mainly in intestine and muscle on the second and third day after exposure whereas starvation-induced increase in catabolism occurs primarily in the liver and on the first day of starvation.

L6 ANSWER 21 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1960:120119 CAPLUS  
DOCUMENT NUMBER: 54:120119  
ORIGINAL REFERENCE NO.: 54:23006e-g  
TITLE: Histamine metabolism in human disease  
AUTHOR(S): Beall, Gildon N.; Van Arsdel, Paul P., Jr.  
CORPORATE SOURCE: Univ. of Washington, Seattle  
SOURCE: Journal of Clinical Investigation (1960), 39, 676-83  
CODEN: JCINAO; ISSN: 0021-9738  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable

AB The metabolism of histamine-C14 was studied in 7 control subjects, 5 patients with Laennec's cirrhosis, 3 with bronchial asthma, 3 with histaminic cephalgia, and 1 with uremia due to chronic glomerulonephritis. Radioactive histamine was always rapidly cleared from the blood, and its excretion was usually complete in 30 hrs. Sepn. of the excreted radioactive metabolites by paper chromatography and radioautography showed **imidazoleacetic** acid to be the principal product of histamine metabolism. **Imidazoleacetic** acid riboside and 1,4-methylimidazoleacetic acid were also consistently recovered in the urine, but histamine-C14 was not detected. Histamine inactivation and degradation in man is a rapid and complete process and, by the methods employed, no abnormalities were found in the diseases studied. 25 references.

L6 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1959:28685 CAPLUS  
DOCUMENT NUMBER: 53:28685  
ORIGINAL REFERENCE NO.: 53:5140c-e  
TITLE: Synthesis of 1-.beta.-D-ribofuranosyl-4(5)-glyoxalinyllacetic acid, a metabolite of histamine  
AUTHOR(S): Baddiley, J.; Buchanan, J. G.; Hayes, D. H.; Smith, P. A.  
CORPORATE SOURCE: Univ. Durham, Newcastle-upon-Tyne, UK  
SOURCE: Journal of the Chemical Society, Abstracts (1958) 3743-5  
CODEN: JCSAAZ; ISSN: 0590-9791  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable

AB A synthesis is described which established the configuration of the ribosyl linkage: the HgCl2 salt of Me 4-glyoxalinyll acetate is condensed with tri-O-benzoyl-.beta.-D-ribofuranosyl chloride in boiling xylene, the product debenzoylated, and the Me ester group hydrolyzed. The ribosyl compd. is isolated by ion-exchange chromatography. Comparison with the natural compd. (m.p., infrared spectrum, RF values in various solvent systems, and behavior on acid hydrolysis) proves their identity. Reaction of a tri-O-acetyl- or tri-O-benzoylribofuranosyl halide with Hg salts

yields only the .beta.-anomer in all cases so far studied. This established the .beta.-configuration of the natural product.

L6 ANSWER 23 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1959:24133 CAPLUS

DOCUMENT NUMBER: 53:24133

ORIGINAL REFERENCE NO.: 53:4472f

TITLE: Isolation of **imidazoleacetic** acid riboside

AUTHOR(S): Tabor, H.

CORPORATE SOURCE: Natl. Inst. of Arthritis and Metabolic Diseases, Bethesda, MD

SOURCE: Ciba Foundation Symposium, Histamine (1956) 51

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB Reviews with many references.

L6 ANSWER 24 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1959:12622 CAPLUS

DOCUMENT NUMBER: 53:12622

ORIGINAL REFERENCE NO.: 53:2404a-c

TITLE: Ribose metabolism. V. Factors influencing in vivo ribose synthesis in the rat

AUTHOR(S): Hiatt, Howard H.

CORPORATE SOURCE: Harvard Med. School, Boston, MA

SOURCE: Journal of Clinical Investigation (1958), 37, 1453-60  
CODEN: JCINAO; ISSN: 0021-9738

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. C.A. 52, 16519c. Ribose synthesis in vivo was studied by isolating **imidazoleacetic** acid (IZA) riboside from rats given IZA and a C14-labeled sugar. Evidence is presented which indicates an impairment of riboside excretion in partially hepatectomized animals and in diabetic animals. The isotope distribution in ribose synthesized from glucose-2-C14 by normal animals is consistent with synthesis via both the oxidative and the nonoxidative reactions of the pentose phosphate pathway. Thiamine deficiency resulted in a marked decrease of ribose synthesis from hexose via the nonoxidative mechanism. An apparent increase in ribose production by way of the oxidative reactions was observed in rats with regenerating livers and in tumor-bearing rats. Evidence is presented for the direct incorporation of administered ribose into the urinary riboside.

L6 ANSWER 25 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1957:52995 CAPLUS

DOCUMENT NUMBER: 51:52995

ORIGINAL REFERENCE NO.: 51:9851f-h

TITLE: The metabolism of histamine in various species

AUTHOR(S): Schayer, Richard W.

CORPORATE SOURCE: Rheumatic Fever Research Inst., Chicago

SOURCE: British Journal of Pharmacology and Chemotherapy (1956), 11, 472-3  
CODEN: BJPCAL; ISSN: 0366-0826

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. C.A. 50, 14838a. Quant. analyses for histamine (I) metabolites in urine of various species after feeding or injecting I-C14 were performed. In the rabbit, I was equally metabolized by oxidation and by methylation to give 1-methylimidazole-4-acetic acid (II) and 1-ribosylimidazole-4(5)-acetic acid (III). The mouse metabolized fed I to III plus some **imidazole-4-acetic** acid and II. In cats and man methylation was the principal route of metabolism for fed or injected I to give II. The cat excreted some unchanged I. The dog excreted injected I as II together with 1-methyl-4-(2-aminoethyl)**imidazole** and 4-**imidazoleacetic** acid. In the cat a small fraction of injected L-histidine-C14 was recovered as tissue I after 8 days; in contrast no

injected I-C14 was retained.

L6 ANSWER 26 OF 26 MEDLINE on STN  
ACCESSION NUMBER: 95341318 MEDLINE  
DOCUMENT NUMBER: 95341318 PubMed ID: 7616240  
TITLE: **Imidazoleacetic** acid, a gamma-aminobutyric acid  
receptor agonist, can be formed in rat brain by oxidation  
of histamine.  
AUTHOR: Thomas B; Prell G D  
CORPORATE SOURCE: Department of Pharmacology, Mount Sinai School of Medicine,  
City University of New York, New York, USA.  
CONTRACT NUMBER: NS 28012 (NINDS)  
SOURCE: JOURNAL OF NEUROCHEMISTRY, (1995 Aug) 65 (2) 818-26.  
Journal code: 2985190R. ISSN: 0022-3042.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199508  
ENTRY DATE: Entered STN: 19950905  
Last Updated on STN: 19980206  
Entered Medline: 19950824

AB It is generally accepted that in mammalian brain histamine is metabolized solely by histamine methyltransferase (HMT), to form tele-methylhistamine, then oxidized to tele-methylimidazoleacetic acid. However, histamine's oxidative metabolite in the periphery, **imidazoleacetic** acid (IAA), is also present in brain and CSF, and its levels in brain increase after inhibition of HMT. To reinvestigate if brain has the capacity to oxidize histamine and form IAA, conscious rats were injected with [3H]histamine (10 ng), either into the lateral ventricles or cisterna magna, and decapitated 30 min later. In brains of saline-treated rats, most radioactivity recovered was due to tele-methylhistamine and tele-methylimidazoleacetic acid. However, significant amounts of tritiated IAA and its metabolites, IAA-ribotide and IAA-riboside, were consistently recovered. In rats pretreated with metoprine, an inhibitor of HMT, labeled IAA and its metabolites usually comprised the majority of histamine's tritiated metabolites. [3H]Histamine given intracisternally produced only trace amounts of oxidative metabolites. Formation of IAA, a potent GABA-A agonist with numerous neurochemical and behavioral effects, from minute quantities of histamine in brain indicates a need for reevaluation of histamine's metabolic pathway or pathways in brain and suggests a novel mechanism for interactions between histamine and the GABAergic system.

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